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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY AND POLUTION PREVENTION/OFFICE OF PESTICIDE PROGRAMS

MEMORANDUM

DATE: September 14, 2010 SEP 14 2010

SUBJECT: Review of Registrant Response to Deficiency Letter in Support of the Registration of *Moss Buster*, Containing 1.0 % Oregano Oil (from *Origanum vulgar*) As Its Active Ingredient.

Decision Number:	**384851**
DP Number:	**378442**
EPA File Symbol Number:	**84316-R**
Chemical Class:	**Biochemical**
PC Code:	**004300**
CAS Number:	**8007-11-2**
Active Ingredient Tolerance Exemptions:	**Non-Food Use**
MRID Numbers:	**47826101, 47826102**
Specific Type of Review:	**Product Chemistry, Toxicology (Human & Non-Target)**

FROM: *Sadaf Shaukat, Biologist*
Biochemical Pesticides Branch
Biopesticides & Pollution Prevention Division (7511P)

TO: *Leonard Cole, Regulatory Action Leader*
Biochemical Pesticides Branch
Biopesticides & Pollution Prevention Division (7511P)

ACTION REQUESTED

In response to the request for additional information discussed in a memorandum from Sadaf Shaukat to Leonard Cole dated 2/10/10 and relayed in a letter from BPPD to the registrant dated 3/12/10, the registrant has submitted a letter dated 4/10/10 attempting to address all deficiencies, including a revised Confidential Statement of Formula (CSF) dated 4/9/10, revised product chemistry data (Exhibit 2-7), and revised human health and non-target toxicology data (Exhibit 8). This memorandum is a review of the registrant response to all cited deficiencies.

Oregano Oil (from *Origanum vulgar*)
PC Code: 004300

DP Number: 378442
EPA File Symbol No.: 84316-R

RECOMMENDATIONS AND CONCLUSIONS

1. The product chemistry submission is UNACCEPTABLE, but upgradeable pending resolution of deficiencies listed below. (Exhibit 1-7)

a. The name of the active ingredient on the CSF and product label must be identical. The CSF lists the active ingredient as "Oregano Oil (Origanum vulgare)" and the product label lists it as "Organic Essential Oil-Oregano: Turkish Source."

b. Quality control methods/techniques must be provided for the production and formulation process of the EP. (OPPTS Guideline 880.1200)

c. Two of the samples in the preliminary analysis (specifically lot# 66326 and #66328) are higher than the upper certified limit for the active ingredient. The registrant must provide an explanation as to why these samples exceed the limit.

d. The purpose of the preliminary analysis is to identify impurities from batch to batch and ensure that they are within the certified limits. The following components of the preliminary analysis are missing and must be provided by the registrant (see EPA Product Properties Test Guideline: OPPTS 830.1700):

    1. Summary and Introduction: Scope and Source of Method
    2. Materials and Methods: Equipment, Reagents and Standards, Detailed Analytical Procedure
    3. Results and Discussion: Accuracy and Precision, Limits of Detection and Quantification
    4. Conclusions: Applicability of Analytical Procedure

e. Results of one-year storage stability and corrosion characteristics studies must be submitted for the EP. (OPPTS 830.6317, 830.6320)

f. Physical and chemical characteristics were submitted for the EP, however they are also required for the TGAI. The registrant must submit this information for the TGAI.

2. **The human toxicology submission is UNACCEPTABLE to satisfy all Tier 1 human health data requirements. The deficiencies listed below must be adequately addressed in order to upgrade to *acceptable*. (MRID 47826102)**

Studies and/or scientifically-credible rationale were **not** submitted to support the following Tier I data requirements (40 CFR 158.2050). These requirements must be fully addressed:

Acute Dermal Toxicity (OPPTS Guideline 870.1200)
Acute Dermal Irritation (OPPTS Guideline 870.2500)

Skin Sensitization (OPPTS Guideline 870.2600)
Acute Inhalation Toxicity (OPPTS Guideline 870.1300)
Bacterial Reverse Mutation Testing (OPPTS Guideline 870.5100)
In vitro Mammalian Cell Assay (OPPTS Guideline 870.5300)

a. Information provided to fulfill the requirements for **acute dermal toxicity data (OPPTS 870.1200), acute dermal irritation data (OPPTS 870.2500),** and **skin sensitization data (OPPTS 870.2600)** is insufficient. The Agency requested a credible reference/citation for the claim that oregano oil is highly volatile. A clear and valid reference that confirms that oregano oil is highly volatile would have fulfilled the above three data requirements. The registrant submitted Exhibits 4, 5, and 6 to address this deficiency. However, none of these exhibits demonstrate that oregano oil is highly volatile. On the contrary, Exhibit 4 shows that oregano oil's volatility is very low. (VP: 0.0232 mm Hg at 25 deg C) Both exhibits 5 and 6 have no reference to oregano oil's volatility. The registrant should submit studies that follow OPPTS guidelines referenced above to fulfill the data requirements.

b. Information provided to fulfill the requirement for **acute inhalation toxicity data (OPPTS 870.1300)** is insufficient. The Agency requested a valid reference for the vapor pressure of oregano oil. The registrant submitted Exhibit 5 to address this deficiency, however no reference to vapor pressure was found in Exhibit 5. In Exhibit 4, vapor pressure was shown to be quite low for oregano oil. The registrant should submit an inhalation study that follows OPPTS guidelines in order to fulfill this data requirement.

c. Information provided to fulfill the requirement for **bacterial reverse mutation testing (OPPTS 870.5100)** and the ***in vitro* mammalian cell assay (OPPTS 870.5300)** is insufficient. The Agency requested a valid reference and/or citation for the claim that the amount of oregano oil in spices is 3-5%. A valid reference for this claim would have fulfilled the above two data requirements. The registrant submitted Exhibit 7, which does not even address this claim. Rather, the abstract submitted in Exhibit 7 addresses only carvacrol, and not thymol (the other component of oregano oil).

d. The Agency requested the registrant to provide credible references for the following anecdotal claims.

    a. Oregano oil "degrades in as little time as 45 minutes." (page 4/recurring)
    b. "...Pfizer, has a product that is 100% oil of oregano...carvacrol level on that product is listed as over 80%...dose rate orally of 50 mg/day." (page 27-28)

The registrant's response to the first statement was also anecdotal, stating that oregano oil is a "top note oil." In order for the Agency to accept this statement, a credible reference must be provided. As for the registrant's response to the second claim, the registrant

states that Pfizer no longer has this product. The registrant must remove the original claim which is still present on page 31 of Exhibit 8.

3. **The non-target toxicology submission is UNACCEPTABLE to satisfy all Tier 1 non-target requirements. The deficiencies listed below must be adequately addressed in order to upgrade to *acceptable*. (Exhibit 8)**

Studies and/or scientifically-credible rationale were **not** submitted to support the following Tier I data requirements (40 CFR 158.2060). These requirements must be addressed:

Nontarget Insect Testing (OPPTS Guideline 850.4350)
Seedling Emergence (OPPTS Guideline 850.4100)
Vegetative Vigor (OPPTS Guideline 850.4150)

a. Insufficient rationale was provided to fulfill the requirements for **seedling emergence** and **vegetative vigor (OPPTS 850.4100/4150).** The Agency requested that the registrant submit scientifically-valid reference/citation to support the claim that Moss Buster is a selective herbicide. In the registrant response, it is indicated that there may be transient adverse effects to non-target plants. The registrant refers to unpublished studies that would provide more details. The registrant must submit this unpublished data in order for the Agency to properly assess risk to non-target plants. When an assessment concludes that a pesticide's use "may affect" a listed species or its designated critical habitat, the Agency will consult with the U.S. Fish and Wildlife Service and/or National Marine Fisheries Service (the Services), as appropriate.

b. Insufficient information was provided to fulfill the data requirement for **non-target insect testing (OPPTS 850.4350)**. Data or scientifically-credible information must be submitted in order to complete requirements for registration. The registrant states on page 30 of Exhibit 8 that "During field trials with Moss Buster, the company confirmed that the product was sprayed on non-target insects with no adverse results." The registrant must submit data from these field trials in order for the Agency to adequately assess the risk to non-target insects.

Note to RAL:

1. Under the "Directions for Use" section, specifically following "Precautions..." the label language states "may want" in respect to wearing gloves and protective eyewear. This should be changed to "must" in order to be consistent with PPE requirements also on the label.

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STUDY SUMMARIES

Product Chemistry (MRID 47826101)

Oregano Oil is the active ingredient in the end use product, Moss Buster. The CSF and product label are in agreement regarding the active ingredient content. The name of the active ingredient on the CSF does not match the name given on the product label. The formulation process for the EP was provided, however quality control measures were not provided. Results from a five-batch preliminary analysis were provided, however two of the samples exceeded the upper certified limit. The physical/chemical characteristics were adequately presented for the EP, however they were not provided for the TGAI. Storage stability and corrosion characteristics data were not submitted for the EP. (not required for TGAI)

Toxicity

Human Health Assessment

Study Type/OPPTS Guideline	LD_{50}/LC_{50}/Results	Toxicity Category	MRID
Acute Dermal Toxicity/OPPTS 870.1200	Info. to support tox data requirements submitted	Need Reference/Citation/ Study	Exhibit 8
Acute Inhalation Toxicity/OPPTS 870.1300	Info. to support tox data requirements submitted	Need Reference/Citation/ Study	Exhibit 8
Acute Dermal Irritation/OPPTS 870.2500	Info. to support tox data requirements submitted	Need Reference/Citation/ Study	Exhibit 8
Skin Sensitization/OPPTS 870.2600	Info. to support tox data requirements submitted	Need Reference/Citation/ Study	Exhibit 8
Bacterial Reverse Mutation Testing/OPPTS 870.5100	Info. to support tox data requirements submitted	Need Reference/Citation/ Study	Exhibit 8
In vitro Mammalian Cell Assay/OPPTS 870.5300	Info. to support tox data requirements submitted	Need Reference/Citation/ Study	Exhibit 8

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Non-Target Toxicity

Non-Target Organism Assessment

Study Type/OPPTS Guideline	LD_{50}/LC_{50}/Results	Toxicity Category	MRID
Nontarget Insect Testing/OPPTS 850.4350	Info. to support tox data requirements submitted	Need Reference/Citation/ Study	Exhibit 8
Seedling Emergence/OPPTS 850.4100	Info. to support tox data requirements submitted	Need Reference/Citation/ Study	Exhibit 8
Vegetative Vigor/OPPTS 850.4150	Info. to support tox data requirements submitted	Need Reference/Citation/ Study	Exhibit 8

cc: *S. Shaukat, L. Cole*, BPPD Science Review File, IHAD/ARS
S. Shaukat, FT, PY-S: *9/14/10*

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Chemical Name:

PC Code:
HED File Code: 41500 BPPD Tox/Chem
Memo Date: 9/14/2010
File ID: 00000000
Accession #: 000-00-0137

HED Records Reference Center
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